Patients' information-seeking activity is associated with treatment compliance in inflammatory bowel disease patients

Pittet, Valérie ; Rogler, Gerhard ; Mottet, Christian ; Froehlich, Florian ; Michetti, Pierre ; de Saussure, Philippe ; Burnand, Bernard ; Vader, John-Paul ; Swiss IBD Cohort Study Group

Abstract: BACKGROUND: Despite the chronic and relapsing nature of inflammatory bowel diseases (IBD), at least 30% to 45% of the patients are noncompliant to treatment. IBD patients often seek information about their disease. AIM: To examine the association between information-seeking activity and treatment compliance among IBD patients. To compare information sources and concerns between compliant and noncompliant patients. METHODS: We used data from the Swiss IBD cohort study, and from a qualitative survey conducted to assess information sources and concerns. Crude and adjusted odds ratios (OR) for noncompliance were calculated. Differences in the proportions of information sources and concerns were compared between compliant and noncompliant patients. RESULTS: A total of 512 patients were included. About 18% (n = 99) of patients were reported to be noncompliant to drug treatment and two-thirds (n = 353) were information seekers. The OR for noncompliance among information seekers was 2.44 (95%CI: 1.34-4.41) after adjustment for confounders and major risk factors. General practitioners were 15.2% more often consulted (p = 0.019) among compliant patients, as were books and television (+13.1%; p = 0.048), whereas no difference in proportions was observed for sources such as internet or gastroenterologists. Information on tips for disease management were 14.2% more often sought among noncompliant patients (p = 0.028). No difference was observed for concerns on research and development on IBD or therapies. CONCLUSION: In Switzerland, IBD patients noncompliant to treatment were more often seeking disease-related information than compliant patients. Daily management of symptoms and disease seemed to be an important concern of those patients.

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Patients' information-seeking activity is associated with treatment compliance in inflammatory bowel disease patients

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Short title: Non-compliance-to-treatment and information concerns

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ABSTRACT

Background: Despite the chronic and relapsing nature of inflammatory bowel diseases (IBD), at least 30 to 45% of the patients are non-compliant to treatment. IBD patients often seek information about their disease.

Aim: To examine the association between information seeking activity and treatment compliance among IBD patients. To compare information sources and concerns between compliant and non- compliant patients

Methods: We used data from the Swiss IBD cohort study, and from a qualitative survey conducted to assess information sources and concerns. Crude and adjusted odds ratios (OR) for non-compliance were calculated. Differences in the proportions of information sources and concerns were compared between compliant and non-compliant patients.

Results: 512 patients were included. Eighteen percent (N=99) reported to be non-compliant to drug treatment and two thirds (N=353) were information seekers. The OR for non-compliance among information seekers was 2.39 (95%CI 1.32-4.34) after adjustment for confounders and major risk factors. General practitioners were 15.2% more often consulted (p=0.019) among compliant patients, as were books and TV (+13.1%; p=0.048) while no difference in proportions was observed for sources such as internet or gastroenterologists. Information on tips for disease management were 14.2% more often sought among non-compliant patients (p=0.028). No difference was observed for concerns on research and development on IBD or therapies.

Conclusion: In Switzerland, IBD patients non-compliant to treatment were more often seeking disease-related information than compliant patients. Daily management of symptoms and disease seemed to be an important concern of those patients.

KEYWORDS

Crohn's disease, ulcerative colitis, information seeking, information concerns, compliance to treatment

INTRODUCTION

Inflammatory bowel diseases (IBD), comprising Crohn's disease (CD) and ulcerative colitis (UC) are mostly diagnosed at young age, implying a lifelong duration of disease with relapsing acute phases followed by periods of remission (1). Phases and their duration are not predictable, and their frequency, severity and treatment vary largely among patients, impacting on daily living and quality of life. Most patients require long-term and multiple therapy regimens and about 70% of CD patients require respective bowel surgery.

Despite the known risk of recurrence, 7 to 72% of IBD patients reported to be non-adherent to treatments (2), with a mean varying between 30% and 45%, during maintenance of remission. Previous studies showed the proportion of adherent patients to be generally higher in CD as compared to UC (2-4), because of the need for more regular medical visits, with increased contact and communication. Risk factors for non-adherence were of different types: socio-demographic, psychosocial, disease-related, information- or knowledge-related. Younger age, being male or single or having a full-time daily activity were related to non- or low- adherence (2, 5-7); income or deprivation scores showed no association (5). Distress, anxiety, perceived stress and well-being showed conflicting results (5, 7, 8). Disease duration, location and activity as well as a recent diagnosis and infrequent visits to physician were related to non-compliance (4, 9). In addition, drug-related factors such as type of drugs, burden of drug regimens, multiple therapies, and complicated dosage regimens increased the risk of forgetfulness (2, 4, 10). The first studies investigating IBD patient's information needs in the 70's to 90's showed concerns focused on aetiology, symptoms, diet, and on

therapies and their related risks and benefits (11-15). Low information and support were associated with non-adherence to treatment (16, 17). Kane assumed that improving the information that physician may give to patients concerning drugs and their use would increase adherence (6). Beliefs about medications and doctor-patient discordance on beliefs were found to be associated with low adherence (2), but trust-in-physician was shown to be highly correlated with adherence (8). Carpenter observed, in a sample of chronically ill patients (18), that one half (51%) of them received conflicting information, a phenomenon requiring further investigation, including the distinction between active and passive ways of gathering information and its impact on treatment adherence.

The effect of being well-informed on potential improvement of the course and management of IBD has been hypothesised, but not well explored. Adherence, which definition supposes there was a patient-physician agreement on the treatment recommendation (19) encloses compliance, defined more crudely as "the extent to which the patient's behaviour matches the prescriber's recommendations". We aimed to investigate the role of patients' information seeking activities on treatment compliance. A secondary objective was to explore and compare sources and themes of information sought by patients with respect to being compliant or non- compliant to treatment.

MATERIALS AND METHODS

Study design and population

This cross-sectional study used data from patients included in the Swiss Inflammatory Bowel Diseases Cohort (SIBDC), a national clinical cohort launched in November 2006. The methods and goals of the study were described elsewhere (20). Briefly, the study enrolled paediatric or adult patients with CD, UC or indeterminate colitis, with a diagnosis having been established for at least four months and confirmed by radiological, endoscopic or surgery assessment. Patients with other forms of colitis, having no permanent residence in Switzerland, or refusing to sign the informed consent form were excluded. Patients were enrolled by their treating gastroenterologist in private or public ambulatory practices and hospitals. The study population consisted of all adult patients included in the cohort study between November 2006 and August 2009, taking at least one drug at baseline, and who responded to a survey on information seeking.

Data collection and management

Clinical data were gathered from gastroenterologists or study nurses through clinical reporting forms during the enrolment medical visit. A self-administered questionnaire was sent to patients by mail following the baseline medical visit. A qualitative survey was developed based on critical incident reporting method (21, 22), and was conducted in October 2009 among patients enrolled up to that time to investigate sources and themes of information searched in four critical stages of the disease. Linkage with SIBDC clinical and patient data was made by using the unique ID number, assigned to all patients included in the cohort.

Outcome and exposures

The studied outcome was "non-compliance to treatment". This measure was study-specifically developed and collected as an unordered categorical variable with 5 categories for each drug therapy taken by the patient. The categories were: "therapy taken according to dosage and frequency prescribed", "therapy taken according to dosage but not always to the frequency", "therapy taken according to frequency but no always to the dosage", "therapy taken according neither to dosage nor to the frequency", "therapy never taken". For the purpose of this study compliance was treated as a binary variable; "compliant" referred to complete respect of dosage and frequency and "non-compliant" to any of the 4 other categories.

Information seeking was studied for two main disease stages, i.e., activity or remission. To investigate the overall association between compliance and information seeking, we first defined exposure as a binary variable (yes/no); "yes" referred to information seeking, whether at the time of disease activity, or of remission, and "no" to no information seeking. Patients were considered as active information seekers if they had sought information in at least one of the two disease stages. For the purpose of this study, we classified patients who did not remember if they sought information (N=6) as non-seekers. Themes of information searched were collected as follows: patients were first asked to check if they had sought information ("yes", "no", "do not remember"), then they were asked to describe the type of information sought through an open-ended question. Content analysis was performed by extracting keywords out of the text from open-ended questions and by grouping them, first in sub-themes then in main themes. A double check of the classifications in sub- and main themes was performed independently by an experienced qualitative researcher. The number of sub- themes

defined was 43, which were grouped in 6 main information themes (Table 1). Each patient could seek information in a single or in multiple themes. To explore the proportion of each theme explored independently we created 6 binary variables, each referring to one of the main themes. Sources patients may have used to gather information on their disease were identified using a pre-established list of six binary variables: "family doctor", "gastroenterologist", "pharmacist", "patient association", "internet", "book" or "TV".

Potential confounders and other risk factors

Potential confounding for the association between compliance and information seeking was explored for the following variables: age, gender, duration of disease, marital status, education level, working status, depression and anxiety scores (23), type of diagnosis, previous surgeries, previous complications, use of alternative medicine, use of nutritional supplements, type of drugs and poly-medication. Marital status was considered as a binary variable, with two categories: "legally married" / "not married". Education level was grouped into 3 categories: "Primary (mandatory) education level", "Secondary education level", and "university level and assimilated". Working status was grouped into 6 categories: "full-time activity", "part-time activity", "unemployed", "in training", "at home", and "retired". Both education and working status classifications derived from these commonly used in the Swiss national health statistics (http://www.bfs.admin.ch/). Drug therapies were treated using two distinct variables: type of drug regimen and number of concomitant drugs. Types of drug regimens were classified taking account of the burden they might place on patients, e.g. potential adverse effects and their severity, burden induced by administration route (topical, oral or intravenous), and for this reason were grouped into the following categories:

"Antibiotics or topical steroids" (metronidazole, ciprofloxacin, topical steroids, budesonide), "5-ASA" (oral and/or topical 5-ASA, sulfasalazine), "oral steroids" (prednisone, systemic steroids), "immunosuppressive drugs" (methotrexate, azathioprine, 6-mercaptopurine), and "biologicals" (infliximab, adalimumab, certolizumab). Diagnosis and clinical characteristics of the disease were taken from the clinical report forms. Duration of disease and patient's age were treated as continuous variables. Disease characteristics were grouped according to the Vienna classification (24).

Statistical analysis

Univariate analyses were performed using logistic regression to examine the strength of the association between compliance to treatment and information seeking, and other exposure variables. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. Statistical significance of the association between compliance to treatment and each factor was assessed using likelihood ratio tests (LRT). To investigate for potential confounding of the association between compliance and information seeking, factors significantly associated with the outcome (LRT < 0.1) were tested for association with the main exposure. Chi-2 test or Fisher's test were used to test for the null hypothesis of no association between variables. A LR test was performed to assess for potential interaction between information seeking and drug regimen. The association between adherence to treatment and information seeking was then controlled for potential confounders using a multivariate logistic regression model. Adjusted OR were compared with crude OR for the effect of information seeking on compliance to assess for the strength of confounding effect. Other strong risks factors identified in previous studies were also controlled for in the final adjusted model. To compare information

seeking sources and themes searched between groups of compliant and non-compliant seekers patients, the proportions of those who consulted each of the 6 different sources, respectively each of the different topics, were calculated with 95% CI. The differences between proportions of those who consulted the source, respectively the theme were calculated and a z-test was performed for testing the null hypothesis of no difference. Results presented in the tables were converted in percentages.

Analyses were conducted using STATA statistical software v.12.1 (STATA Corp. Texas, USA).

Ethics approval

SIBDCS approvals were obtained from the respective regional Swiss Ethics Committees where cohort patients were enrolled.

RESULTS

By October 2009, 1530 adult patients were included in the cohort when we started the survey. 262 (17.1%) patients had to be excluded due to incomplete baseline questionnaires or clinical reports. From the remaining patients, 204 (16.1%) did not take any IBD medication and measures of compliance were missing for 122 (11.5%) patients who took medication. Out of the 942 drug treated patients, with drug and adherence data, 537 (57%) responded to the survey on information seeking. From the 537 respondents, 25 (4.7%) had to be excluded because their answers were incomplete. The number of patients finally analysed in the present study was 512.

Description of the study population

Half of the patients were males; the mean age was 41 years, and median disease duration 7 years (table 2). Half of the patients were married (N=260), and two-thirds (N=339) had a secondary education level. Most patients were working full or part-time (62.1%; N=318). About one out of six patients had moderate to severe anxiety (16.2%; N=83), and one out of fifteen had severe depression (6.5%; N=33). Eighteen percent (N=99) reported to be non-compliant to treatment, and nearly two thirds (N=353) of the patients were seeking information on their disease. Half of the patients suffered from CD, 65.1% (N=183) of them had colonic affections (Table 3). About one third had a fistulizing disease course, which represents the phenotype with the highest burden. Left-sided disease was the most frequent location in UC. One third of IBD patients (N=154) had experienced at least one resection surgery and two-thirds (N=322) >=1 disease-related complication. One third of patients (N=162) used alternative medicines and nearly two-thirds (N=320) used nutritional supplements. Three quarters (N=366) of the patients were under immunosuppressive drug or 5-aminosalicylates, and one out of five

was under biological therapy. Forty-two percent of the patients under drug therapy took at least two concomitant medications.

Correlates of treatment non-compliance

The crude odds of being non-adherent (table 4) was significantly higher among information seekers (69%, p=0.045), and decreased significantly by 3% with each year's increase of age (p<0.001). No strong evidence of association with non-compliance was found for duration of disease, gender, marital and working status, education level, anxiety and depression scores. Crude odds of being non- compliant were 48% lower among patients with a previous history of surgery (p=0.016) or who were using nutritional supplements (p=0.005) (table 5). Factors significantly associated with non-compliance were considered as potential confounders, after checking association between those factors and information seeking. Interaction between information seeking and drug regimen was tested; results showed no evidence of an interaction between these two variables (LRT p-value=0.884).

A first model was fitted which included the two confounding factors (nutritional supplements use and drug regimen), and known risk factors for compliance (age, history of surgery and complications, marital status). Then, further adjustment was made on gender, education level, working status and HADS anxiety and depression scores. This choice was made because these were identified as risk factors for the outcome in previous studies. The adjusted OR for non-compliance was found to be 2.44 among information seekers compared to non-seekers (p=0.003), table 6. There was marginal evidence of an association between adherence and the use of nutritional supplements (p=0.038). Age, taking antibiotics/topical steroids or 5-ASA compounds remained significantly associated with non-compliance.

Analysis of information seeking sources and themes

Gastroenterologists were the most frequent source of information (N=304; 90.7%), followed by the internet (N=250; 74.6%), books or TV (N=143; 42.7%) and family doctor (N=130; 38.8%), figure 1. Patients associations were consulted by 62 patients (18.5%) and pharmacists by 17 (5.1%). Compliant patients mentioned their general practitioner (GP) as a more frequent source of information on IBD than non-compliant patients (p=0.019), as were books or TV. No evidence for a difference in the frequencies of consultation was observed for sources such as internet, gastroenterologists, pharmacists or patients associations. The most frequent information topics searched were “therapy” (N=155; 46.3%), “research and development on IBD” (N=151; 45.1%), and “tips for daily disease management” (N=123; 36.7%). Basic information on the diseases were sought by 17.9% of the patients and 6.9% mentioned they sought sharing of experience. Searching for tips for daily disease management was 14.2% higher in the group of patients non- compliant to treatment compared to the group of patients who were compliant. There was no evidence of a difference among groups for information concerns on research and development on IBD, therapies, basic information on the disease, patients experience sharing or miscellaneous information for non-adherent compared to compliant patients.

DISCUSSION

Nearly one out of five patients was non-compliant to drug treatment and 69% of patients were actively seeking information on their disease. We found that non-compliant patients were 2.44 times more likely to be active information seekers as compared to non-seekers after controlling for confounders and known risks factors for non-compliance. Patients who were compliant to drug treatments mentioned general practitioners to be a source of information significantly more often than non-compliant. They searched 13.1% more often information from books or TV. Information topics linked to tips for disease management were significantly of more interest among non-compliant patients compared to those who were compliant.

The majority of patients' compliant to their drug treatments did not search for additional information, which may be interpreted as an overall satisfaction, in terms of information needs. Alternatively, some patients may be compliant to treatment without asking detailed information about treatment rationale, expected benefits and possible adverse events. Secondly, we observed that overall information seeking was strongly associated with non-compliance to treatment. Although the design of our study does not allow conclusions on the cause of this association, this may indicate that non-compliant patients have different needs in terms of information on their disease compared to compliant patients. Information seeking therefore is an important issue to consider. In other chronic diseases such as cancer, studies have shown that patients searching for health-related information were more compliant (25-27). This was not confirmed in the present study with IBD patients; this may have been partly influenced by the specific conditions and course of IBD; indeed mortality rates due to IBD are low (8/10,000)

compared to those observed for cancers and the overall symptomatology is different in inflammatory compared to non-inflammatory chronic diseases. A recent study of Borgaonkar et al. showed that disease-related information seeking had a negative effect on quality of life in IBD (28). Our findings showed that this effect should probably be modulated according to information concerns. Indeed, information topics linked to symptoms and disease management were a major concern for non-compliant patients; information on therapies was an important, but similar, concern for both compliant and non-compliant patients.

The internet was a major a source of information used by three quarters of the study population, but not more frequently by non-compliant compared to compliant patients. This confirms the frequent use of internet, despite known problems with the quality of information provided, as recently shown (29-31). The fact that books or TV were frequently mentioned, especially among compliant patients, shows that these were still considered as a valued source of information for patients. Apart from gastroenterologists, the most frequent source of information, general practitioners were also frequently asked about IBD. Our results indicate that there might be a need for improving communication between doctors and patients, and so between gastroenterologists and patients, at least in Switzerland. If patients seek for information, they need to find answers, not only in terms of risks, benefits of taking their therapies regularly, but also concerning symptoms and everyday disease management. Findings may suggest that the time doctors take to discuss tips for daily disease management should be considered as a central point. Kane (6) suggests that dialogues with patients during medical visits could be seen as too time-consuming for the physician, but are important in terms of explaining in an appropriate manner to the patient issues

concerning, for example, drug information. Physicians should not overestimate the level of knowledge of patients neither on drugs instructions, nor on the disease itself (32, 33). Actual time available for information activity is probably differently shared by a general practitioner compared to a gastroenterologist, who needs to perform technical acts more often. Results tend however to suggest and appeal for an increased integrative healthcare approach for IBD patients, including physicians from different specialties, but also pharmacists, or IBD nurses which do currently not exist in Switzerland.

The innovative character of this study is the use of clinical and patient data from an already established national clinical cohort, with patients enrolled throughout the country and followed in diverse settings. This allowed us to capture a picture regarding compliance to treatment and information concerns at a national level, which is important regarding future communication issues. The use of open questions to gather information on themes searched was another strength of the study as this allowed exploring answers in a way which has not been previously done. Information on compliance to treatments is generally not easy to collect, as shown previously (6, 19, 34). In the SIBDC, we decided to collect compliance to treatment via self-reported patient questionnaires using a local scale, not the standard validated ones used to measure adherence. We understand this may be a limitation of our study. Although compliance was measured using closed questions, we could not avoid potential recall bias from patients that may have reported compliance. One more objective measure of treatment compliance could be made for example, through serum drug levels; this would however not be possible for all treatments. A combination of methods to gather

information on compliance would probably be a future possibility to consider for patients with multiple and complex therapy options like those with IBD.

In comparison to other studies, Swiss IBD patients reported a lower proportion of non-compliance. This may be due to various reasons. Cultural factors may explain the fact that patients from the study population might fear communicating that they did not adhere to their drug regimens, compared to other populations (10) (35). Another reason may be related to the fact that in Switzerland, the number of patients under biological treatments, especially infliximab, is higher than in other countries. Compliance to infliximab should be measured in a different way, as patients need to come for intravenous administration, which is more controlled by the doctors and cannot be avoided, except by not coming to the medical visit (16). We consider information seeking as the overall searching activity spanning different phases of disease activity or remission. It could be argued that this may lead to information bias because patients may be reporting active information seeking in acute phases only, although being in remission for a long time, as mentioned in the patient charts. However, this may be compensated by the fact that overall perception related to the disease was shown to potentially differ between patients and gastroenterologists (32). Indeed, flares and acute symptoms linked to disease activity may be experienced by the patients more often than actually declared to the physician, mainly because concerns linked to one's own disease management differs from that seen through the doctor's eyes. Patients obviously accommodate to their disease over time. We can thus be confident that the way we have taken into account overall information seeking would not lead to strong misclassification.

Selection bias might have occurred due to the high number of non-respondents to the information questionnaire. We investigated therefore the characteristics between both groups with respect to main exposure and risk factors. This showed that non-respondent were somewhat less educated and more often full-time workers, unemployed or retired than responders. They were also slightly more anxious or depressive. Therefore, one might argue that this may affect generalisability of the findings.

In this study, we took into account risks factors that were reported in previous studies. Obviously, there might be some other confounders, known or unknown, which should be taken into account. For example, patient perception of the benefits and risks linked to the drug should also be taken into account because this may differ considerably between subjects.

In conclusion, there is a need to better understand patient beliefs and attitudes, both towards disease and drugs. Better information and communication should be the first step towards improved compliance to treatment and, eventually, better outcomes. Further investigations should be done to confirm these observations. Combining quantitative and qualitative approaches might allow deeper exploration about where deficit of information might be and the potential consequences on treatment compliance. Nevertheless, a take home message for gastroenterologists might be to ask patients explicitly about their information needs and concerns, either directly or with the collaboration of a nurse or through other tools accessible for the patient, e.g., in the waiting room.

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STATEMENT OF AUTHORSHIP

Study design and conception (VP, JPV), statistical analysis (VP), analysis and interpretation (VP, GR, CM, FF, PM, PdS, BB, JPV), drafting the article or revising it critically for important intellectual content (VP, GR, CM, FF, PM, PdS, BB, JPV), final reading and approval of the manuscript (VP, GR, CM, FF, PM, PdS, BB, JPV).

CONFLICTS OF INTEREST

None declared.

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TABLES

Table 1: Details of sub-themes and main themes of information searched

Main themes	**Sub-themes**
Research and development on IBD	Clinical trials
	Origins of the disease
	Hereditary, genetic factors
	Trends in mortality and morbidity
	Epidemiological results / comparison with other countries
	Can we cure the disease?
	Research and development on the disease
	Research and development on new drugs and therapies
Therapies	Comparison between treatments
	Adverse events of drug treatments
	Information on biological treatments
	Information on steroids
	Consequences of stopping / changing drug treatments
	Information on drug medication or other therapies
	Information on surgeries
	Alternative treatments
	Supplementation medicines

Tips for daily disease management	Nutrition
	How to speak to children with the disease
	Risk factors for recurrence of symptoms
	How to prevent recurrence of symptoms?
	Consequences on lifestyle
	Do psychosomatic factors influence the disease?
	Gynaecological aspects
	Pregnancy and babies
	Employment rights and professional activity
	Quality of life
	How to accept the disease status
Patients experience sharing	Exchanges / experiences sharing
	Positive experiences with the disease
	Patients support groups
	TV reports, patients stories, testimonies
Basic information on the disease	All about the disease
	Information on chronic diseases
	Information on complications
	Information on vaccines
	Information on the disease
	Information on gastroenterology
	Cancer
Miscellaneous	Popular information
	Updated information

Information for Swiss people
Information for younger/older

Table 2: Socio-demographic and psychosocial characteristics of the study population. Values are numbers (percentages) unless stated otherwise

Variable	Total	Compliant	Non-compliant
All patients	512 (100.0)	413 (80.7)	99 (19.3)
Age (years)	41 (14) [#]	43 (14) [#]	36 (13) [#]
Duration of disease (years)	7 (12.5) [$]	7 (13) [$]	7 (10) [$]
Information seeking			
No	159 (31.1)	138 (33.4)	21 (21.2)
Yes	353 (68.9)	275 (66.6)	78 (78.8)
Gender			
Men	248 (48.4)	198 (47.9)	50 (50.5)
Women	264 (51.6)	215 (52.1)	49 (49.5)
Marital status			
Not married	252 (49.2)	195 (47.2)	57 (57.6)
Married	260 (50.8)	218 (52.8)	42 (42.4)
Education level			
Primary (mandatory) education level	57 (11.1)	49 (11.9)	8 (8.1)
Secondary education level	339 (66.2)	269 (65.1)	70 (70.7)
University level	112 (21.9)	92 (22.3)	20 (20.2)
Missing value	4 (0.8)	3 (0.7)	1 (1.0)
Working status			
Full-time	197 (38.5)	157 (38.0)	40 (40.4)
Part-time	121 (23.6)	97 (23.5)	24 (24.2)

Unemployed	12 (2.3)	9 (2.2)	3 (3.0)
In training	60 (11.7)	46 (11.1)	14 (14.1)
At home	37 (7.2)	28 (6.8)	8 (9.1)
Retired	78 (15.2)	71 (17.2)	7 (7.1)
Missing value	7 (1.4)	5 (1.2)	2 (2.0)
HADS Anxiety			
Normal	311 (60.7)	248 (60.1)	63 (63.6)
Mild	104 (20.3)	87 (21.1)	17 (17.2)
Moderate	65 (12.7)	51 (12.4)	14 (14.1)
Severe	18 (3.5)	17 (4.1)	1 (1.0)
Missing value	14 (2.7)	10 (2.4)	4 (4.0)
HADS Depression			
Normal	404 (78.9)	322 (78.0)	82 (82.8)
Mild	63 (12.3)	55 (13.3)	8 (8.1)
Moderate	29 (5.7)	25 (6.1)	4 (4.0)
Severe	4 (0.8)	3 (0.7)	1 (1.0)
Missing value	12 (2.3)	8 (1.9)	4 (4.0)

[#] Mean and standard deviation (SD)

[$] Median and inter-quartile range (IQR)

Table 3: Disease- and drug-related characteristics of the study population. Values are numbers (percentages) unless stated otherwise

Variable	Total	Compliant	Non-compliant
All patients	512 (100.0)	413 (80.7)	99 (19.3)
Diagnosis			
Crohn's disease (CD)	281 (54.9)	235 (56.9)	46 (46.5)
Ulcerative colitis (UC)	231 (45.1)	178 (43.1)	53 (53.5)
Disease location (UC only)			
Proctitis	32 (13.8)	20 (11.2)	12 (22.6)
Left-sided	108 (46.8)	86 (48.3)	22 (41.5)
Pancolitis	85 (36.8)	67 (37.6)	18 (34.0)
Unknown	6 (2.6)	5 (2.8)	1 (1.9)
Disease location (CD only)			
Ileal only	67 (23.8)	52 (22.1)	15 (32.6)
Colic only	95 (33.8)	82 (34.9)	13 (28.3)
Ileo-colic	88 (31.3)	75 (31.9)	13 (28.3)
Upper GI	18 (6.4)	16 (6.8)	2 (4.4)
Unknown	13 (4.6)	10 (4.3)	3 (6.5)
Phenotype (CD only)			
Inflammatory	138 (49.1)	107 (45.5)	31 (67.4)
Stenotic	54 (19.2)	47 (20.0)	7 (15.2)
Fistulizing	89 (31.7)	81 (34.5)	8 (17.4)
Previous surgeries			

None	358 (69.9)	279 (77.9)	79 (22.1)
Yes (≥1)	154 (30.1)	134 (87.0)	20 (13.0)
Previous complications			
None	190 (37.1)	144 (34.9)	46 (46.5)
Yes (≥1)	322 (62.9)	269 (65.1)	53 (53.5)
Alternative medicine use			
None	350 (68.4)	278 (67.3)	72 (72.7)
Yes (≥1)	162 (31.6)	135 (32.7)	27 (27.3)
Nutritional supplements			
None	192 (37.5)	142 (34.4)	50 (50.5)
Yes (≥1)	320 (62.5)	271 (65.6)	49 (49.5)
Drug regimen			
Antibiotics or topical steroids	8 (1.6)	5 (1.2)	3 (3.3)
5-ASA	120 (23.4)	82 (19.9)	38 (38.4)
Oral steroids	33 (6.5)	25 (6.1)	8 (8.1)
Immunosuppressive drugs	246 (48.0)	207 (50.1)	39 (39.4)
Biologicals	105 (20.5)	94 (22.8)	11 (11.1)
Number of drugs			
1	299 (58.4)	241 (58.4)	58 (58.6)
2	139 (27.1)	111 (26.9)	28 (28.3)
3	53 (10.4)	43 (10.4)	10 (10.1)
>3	21 (4.1)	18 (4.4)	3 (3.0)

Table 4: Crude OR and 95% CI for non-compliance according to socio-demographic risk factors

Variable	Crude OR (95%CI)	LR test P-value
All patients		
Information seeking		
No	1.00	
Yes	1.69 (0.99 – 2.87)	0.045
Age (years)	0.97 (0.95 – 0.98)	<0.001*
Duration of disease (years)	0.98 (0.96 – 1.01)	0.282
Gender		
Men	1.00	
Women	0.95 (0.60 – 1.50)	0.827
Marital status		
Not married	1.00	
Married	0.68 (0.43 – 1.08)	0.098
Education level		
Primary education level	1.00	
Secondary education level	0.35 (0.15 – 0.85)	
University level	0.45 (0.18 – 1.08)	0.218
Working status		
Full-time	1.00	
Part-time	0.95 (0.53 – 1.70)	

Unemployed	1.35 (0.35 – 5.23)	
In training	1.29 (0.64 – 2.59)	
At home	1.35 (0.56 – 3.24)	
retired	0.40 (0.17 – 0.94)	0.154
HADS Anxiety		
Normal	1.00	
Mild	0.79 (0.44 – 1.43)	
Moderate	1.09 (0.55 – 2.13)	
Severe	0.24 (0.03 – 1.81)	0.312
HADS Depression		
Normal	1.00	
Mild	0.60 (0.28 – 1.32)	
Moderate	0.64 (0.21 – 1.88)	
Severe	1.33 (0.14 – 12.95)	0.490

* P-value for linear trend. Test for departure from linear trend comparing model with age as continuous variable with quartile categories of age showed LRT P-value = 0.868. Therefore, age was considered as a continuous variable.

Table 5: Crude OR and 95% CI for non-compliance according to disease- and drug-related risk factors

Variable	Crude OR (95%CI)	LR test P-value
All patients		
Diagnosis		
Crohn's disease	1.00	
Ulcerative colitis	1.41 (0.89 – 2.22)	0.138
Disease location (UC only)		
Proctitis	2.83 (1.18 – 6.82)	
Left-sided	1.00	
Pancolitis	1.27 (0.61 – 2.62)	0.072
Disease location (CD only)		
Ileal only	1.00	
Colic only	0.59 (0.25 – 1.40)	
Ileo-colic	0.68 (0.29 – 1.58)	
Upper GI	0.46 (0.09 – 2.27)	0.597
Phenotype (CD only)		
Inflammatory	1.00	
Stenotic	0.49 (0.21 – 1.12)	
Fistulizing	0.36 (0.17 – 0.78)	0.006
Previous surgeries		
None	1.00	
Yes (≥1)	0.52 (0.30 – 0.91)	0.016

Previous complications		
None	1.00	
Yes (≥1)	0.64 (0.41 – 1.02)	0.061
Alternative medicine use		
None	1.00	
Yes (≥1)	0.71 (0.43 – 1.19)	0.188
Nutritional supplements		
None	1.00	
Yes (≥1)	0.52 (0.33 – 0.83)	0.005
Drug regimen		
Antibiotics or topical steroids	5.22 (1.08-25.19)	
5-ASA	3.87 (1.80 – 8.29)	
Oral steroids	2.44 (0.84 – 7.05)	
Immunosuppressive drugs	1.58 (0.75 – 3.33)	
Biologicals	1.00	0.001
Number of drugs		
1	1.00	
2	0.96 (0.57 – 1.63)	
3	0.99 (0.47 – 2.10)	
>3	0.49 (0.11 – 2.18)	0.790

Table 6: Odds ratio and 95% CI for non-compliance and information seeking, adjusted for confounding factors and other selected risk factors

Variable	Adjusted OR* 95%CI	Adjusted OR# 95%CI
Information seeking		
No	1.00	1.00
Yes	2.02 (1.15 – 3.57)	2.43 (1.34 – 4.41)
Age (years)	0.96 (0.94 – 0.98)	0.96 (0.94 – 0.99)
Marital status		
Not married	1.00	1.00
Married	0.77 (0.44 – 1.34)	0.67 (0.37 – 1.22)
Previous surgeries		
None	1.00	1.00
Yes (≥1)	0.79 (0.43 – 1.46)	0.80 (0.43 – 1.50)
Previous complications		
None	1.00	1.00
Yes (≥1)	0.91 (0.55 – 1.51)	0.92 (0.54 – 1.55)
Nutritional supplements		
None	1.00	1.00
Yes (≥1)	0.61 (0.38 – 1.02)	0.57 (0.34 – 0.97)
Drug regimen		
Antibiotics or topical steroids	11.31 (2.06 – 62.11)	13.53 (2.31 – 79.02)

5-ASA	4.94 (2.15 – 11.39)	5.27 (2.23 – 12.48)
Oral steroids	2.99 (0.98 – 9.10)	3.28 (1.04 – 10.30)
Immunosuppressive drugs	1.96 (0.91 – 4.23)	1.91 (0.87 – 4.17)
Biologicals	1.00	1.00

*Model 1: adjusted for age, nutritional supplements, marital status, history of surgery, history of complications and drug regimen. #Model 2: additionally adjusted for gender, education level, working status and HADS scores.

FIGURE

Figure 1: Comparison of (A) sources and (B) themes of information consulted among patients compliant and non-compliant to treatment.